

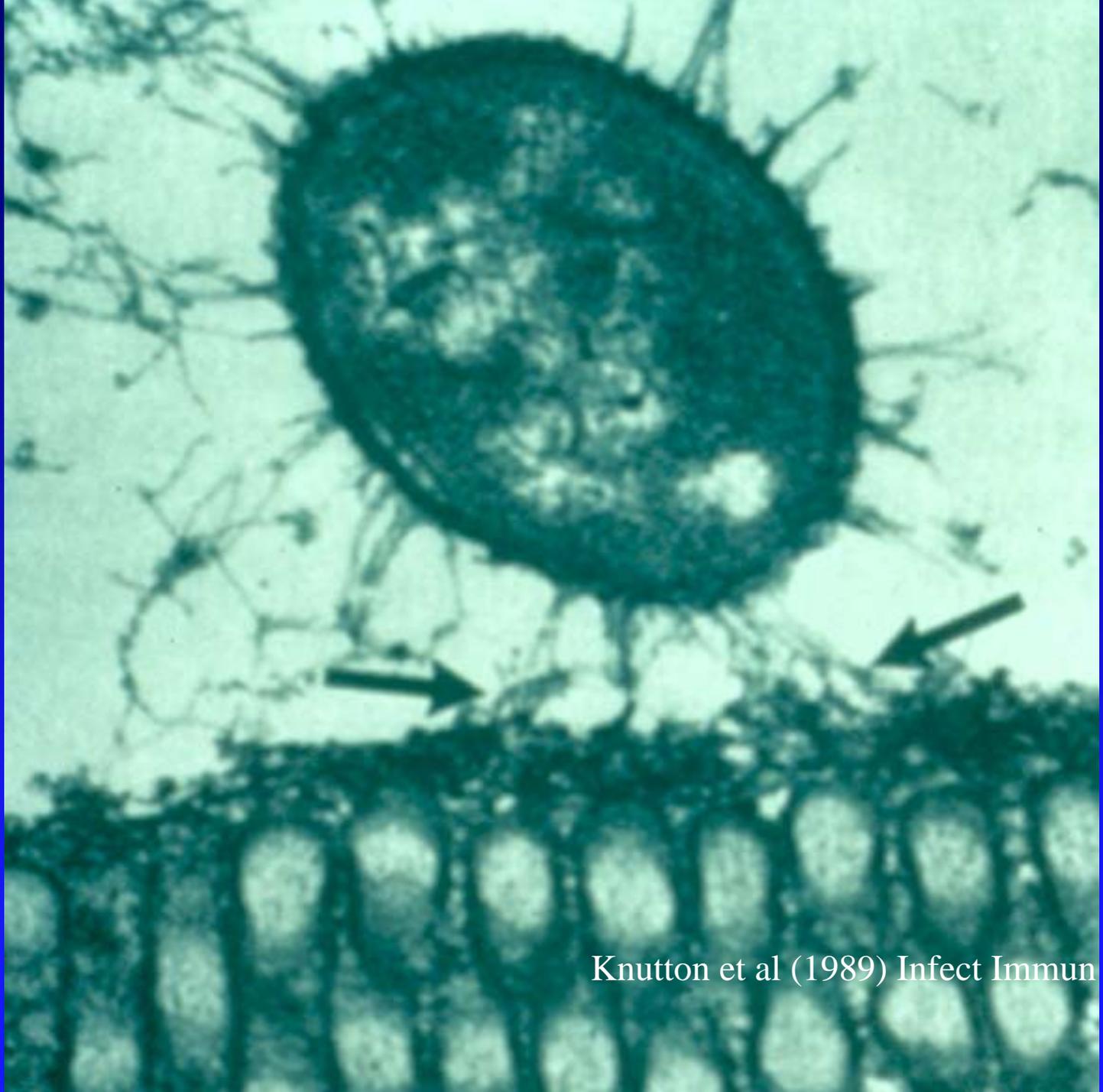
# Vaccine Antigens Encapsulated in Biodegradable, Biocompatible Microspheres for Mucosal Immunization

F. Cassels<sup>1</sup>, E. Hall<sup>3</sup>, A. deLorimier<sup>1</sup>, W. Byrd<sup>1</sup>,  
D. Katz<sup>1</sup>, M. Wolf<sup>1</sup>, and J. van Hamont<sup>2</sup>

Departments of Enteric Infections<sup>1</sup> and Medicinal Chemistry<sup>2</sup>  
Walter Reed Army Institute of Research and  
Department of Enterics<sup>3</sup>, Naval Medical Research Command  
Silver Spring, MD 20910-5100

# Introduction

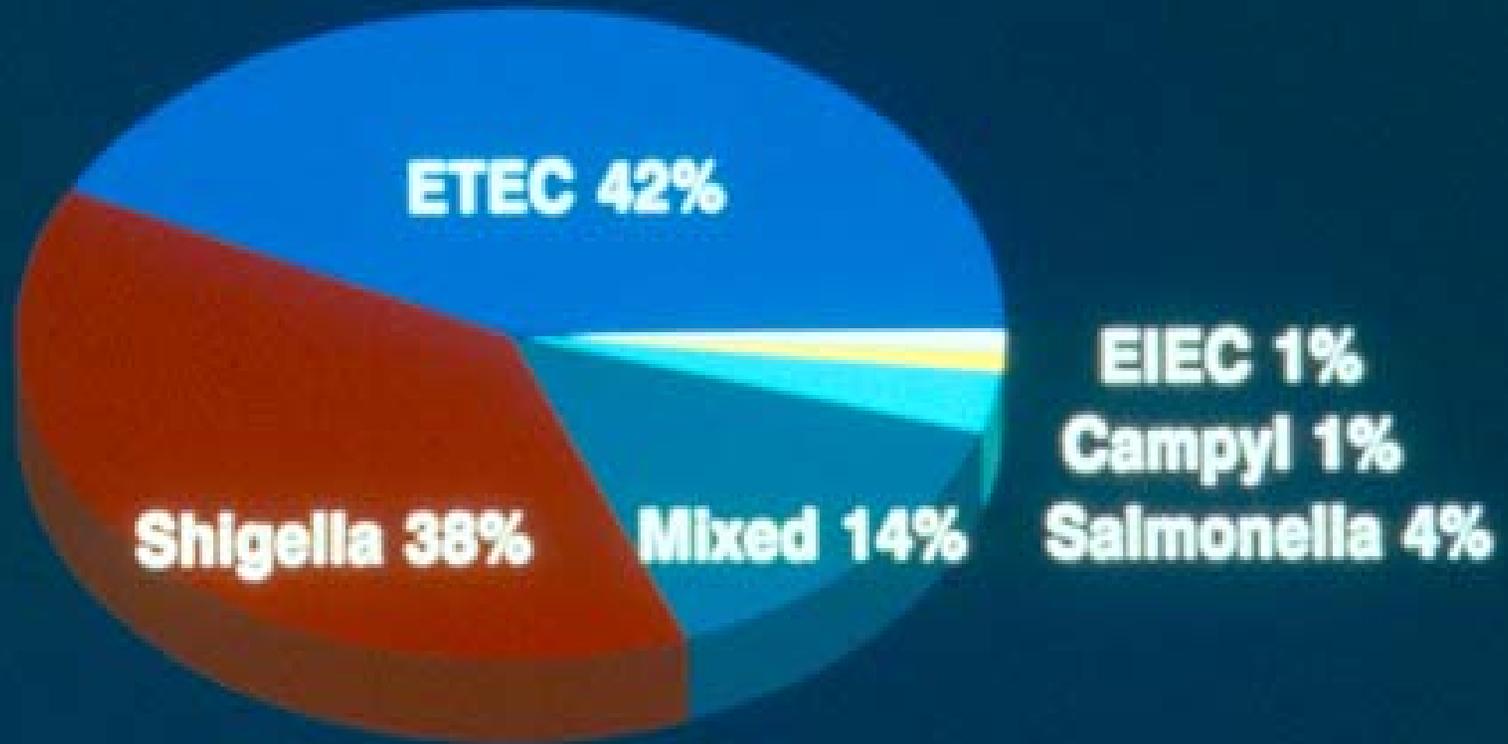
- ETEC Problem
  - Military
  - Travelers
  - Infants in developing countries
- Many ETEC Vaccine Efforts Underway
  - Commonalities: Focus Virulence Factors- CF and LT
  - Differences: Delivery Vehicles, Routes Immunization
    - Oral PLGA Microspheres
    - Skin Patch (Transcutaneous) Immunization
    - Intranasal Immunization
    - Injection (Intramuscular)



Knutton et al (1989) *Infect Immun* 57, 3364

# BACTERIAL ENTEROPATHOGENS

## Saudi Arabia Oct-Dec 1990

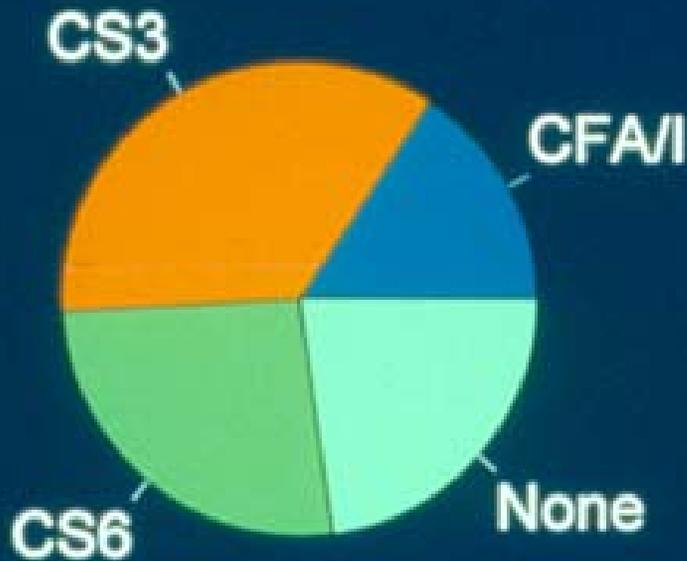


# COLONIZATION FACTOR DISTRIBUTION

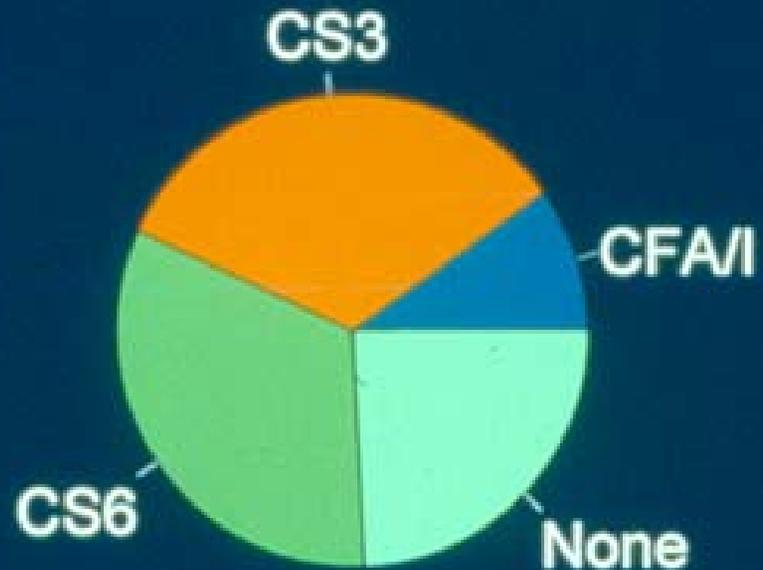
## From U.S. Troops

Egypt 1989

Saudi Arabia 1990

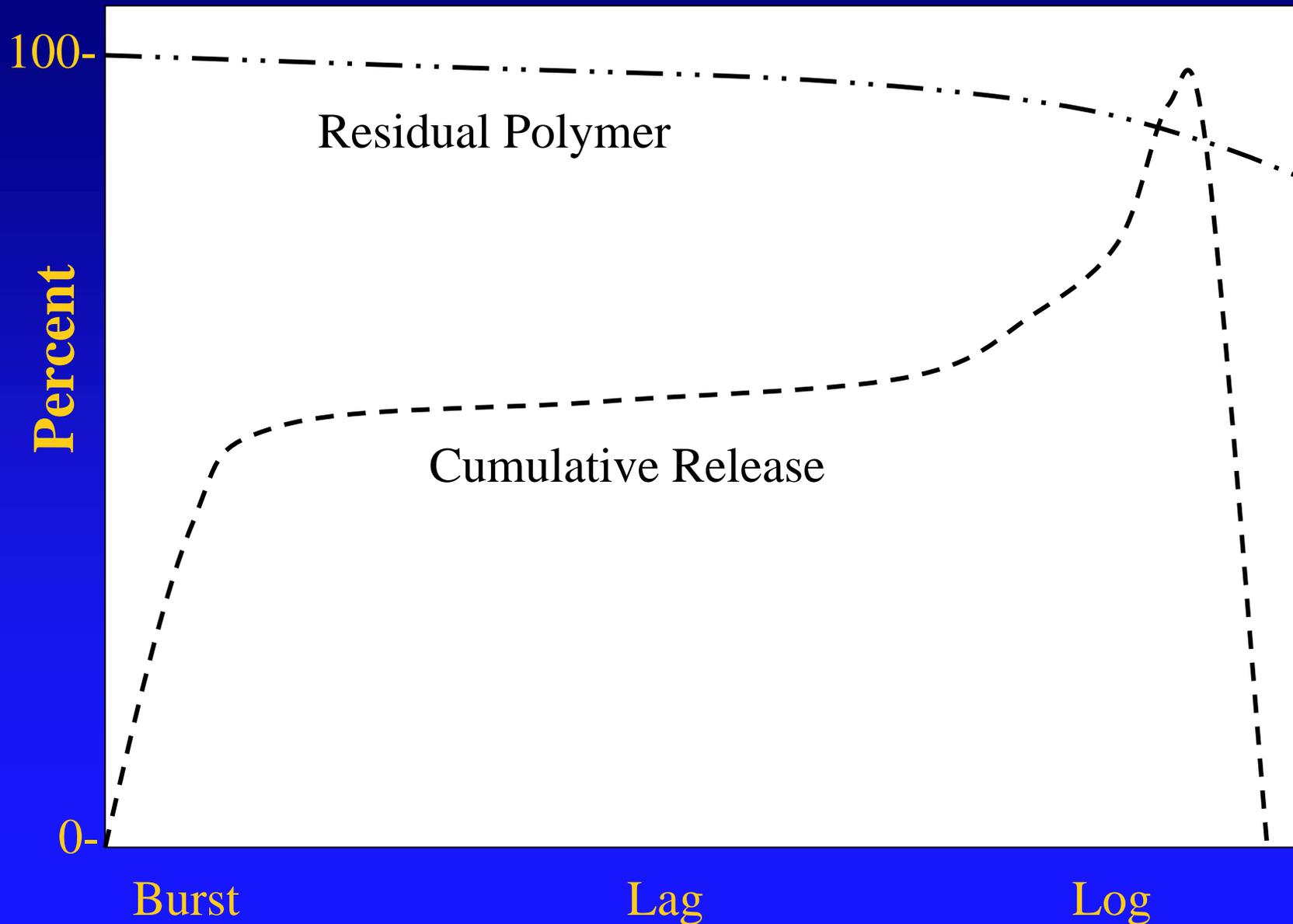


N=57

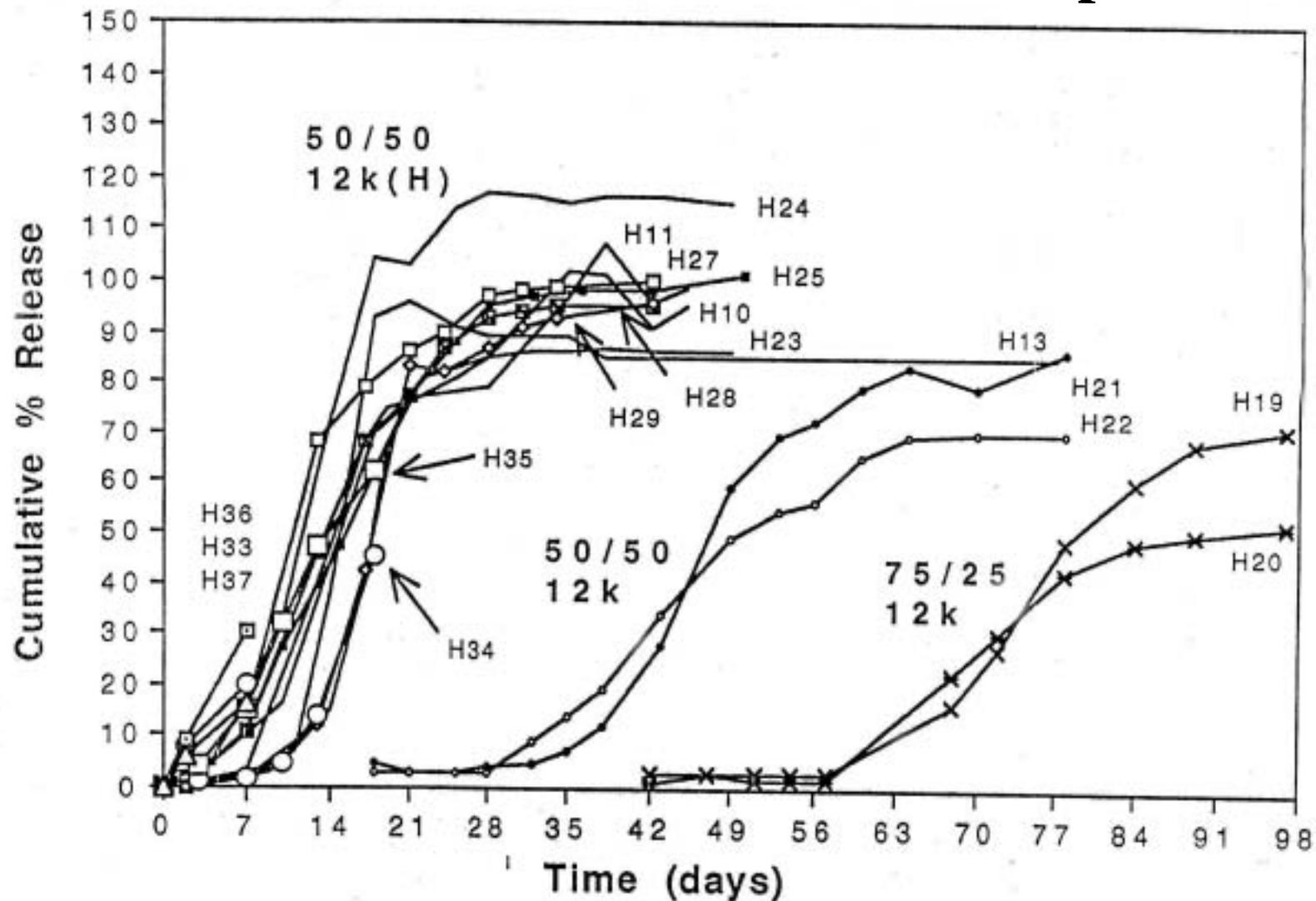


N=132

# Release and Degradation from Conventional Microspheres



# Release from 12K Polymer Microspheres



# PRODUCTION OF CS6 FOR ANIMAL AND HUMAN STUDIES

Cloning and Process Development  
Seed Bank Preparation

Fermentation

Filtration

Precipitation

Microencapsulation

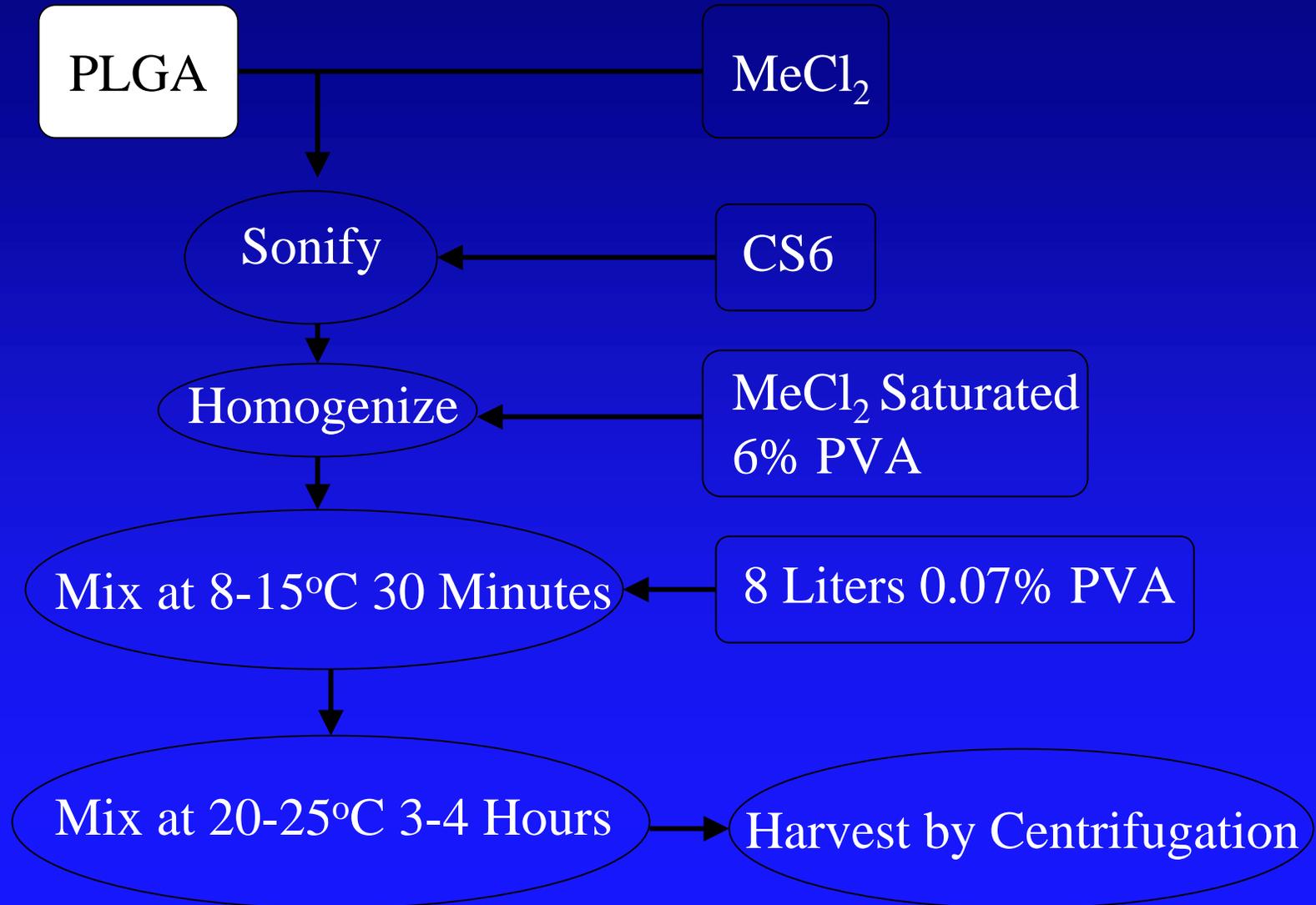
Fill

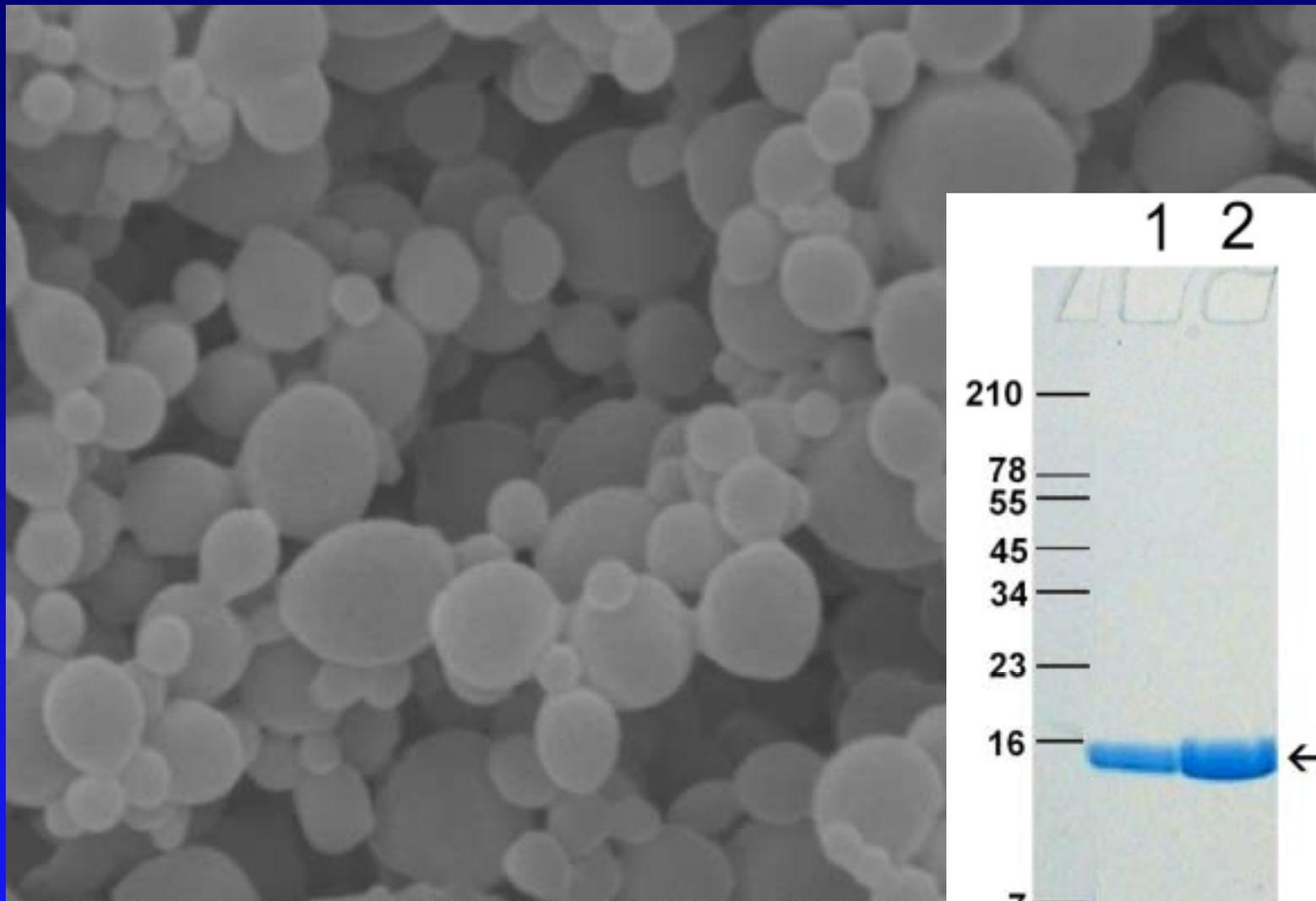


PLGA Microencapsulate  
BPR No.: BPR-223-01  
Contents: N/A  
Cautions: New Drug Label  
to Investigator  
Date of Mfg: 24 May 97  
Manufactured By: WHO

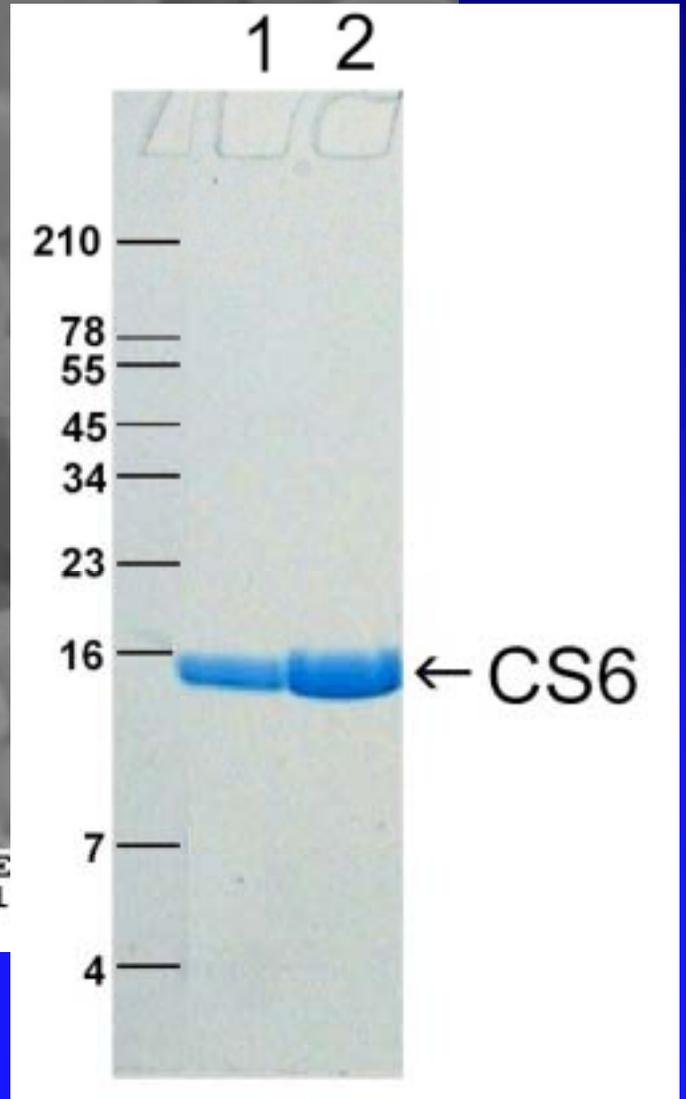
CS6 Vaccine  
BPR No.: D438  
Contents: N/A  
Cautions: For Federal (or United States)  
Use Only  
Storage:  $-80 \pm 10^{\circ}\text{C}$   
Washington D.C. 20307

# Microencapsulation of CS6 by Solvent Evaporation



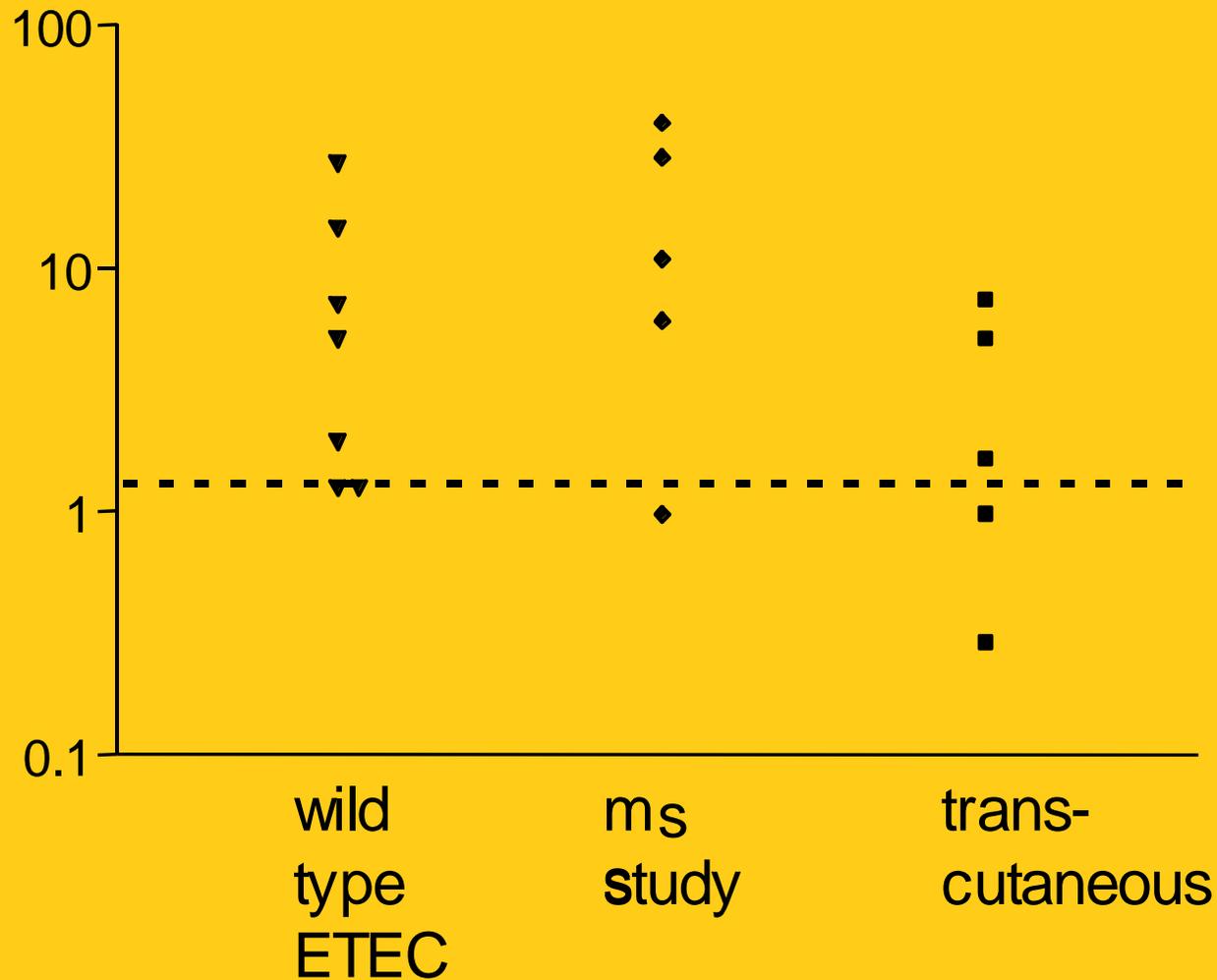


C:\TIFTEST\28JAN99D.TIF CPT VAUGHAN MICROSPE  
Log: 1 Mag=6000 FOU=16.513117 8.0KV 1  
5.00uM



deLorimier et al (2003) Vaccine, in press

# Human Musosal Response to CS6 After Oral Infection, and Immunization with Microspheres and Skin Patch



# Microencapsulated ETEC CS6

- Demonstrated in Animals and Humans
- cGMP Manufactured
- Safe
- Immunogenic: Serum and Mucosal Responses
- Comparable/Better Responses than Challenge  
(likely protected)

# The Army PLGA Microsphere System

- Applicable to Cationic, Neutral and Anionic Molecules
- Programmable Release Up to 100 Days (including burst free)
- Complete Dissolution of Polymer Upon Release
- Can be Buffered to Preserve Biological Activity
- High Loading Efficiencies

# Contact Information

- Frederick J. Cassels, PhD  
Department of Enteric Infections  
WRAIR  
503 Robert Grant Avenue  
Silver Spring, MD 20910  
Phone 301-319-9798  
Fax 301-319-9801  
Email [fred.cassels@na.amedd.army.mil](mailto:fred.cassels@na.amedd.army.mil)

John van Hamont, PhD  
Department of Medicinal Chemistry  
WRAIR  
503 Robert Grant Avenue  
Silver Spring, MD 20910  
Phone 301-319-7399  
Email [john.vanhamont@na.amedd.army.mil](mailto:john.vanhamont@na.amedd.army.mil)